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3D Engineering PEG-Diacrylate hydrogels for mimicking human mechanical microenvironments

Rie Kjær Christensen, Sandra Wilson, Peder Skafte-Pedersen, Niels Bent Larsen

INTRODUCTION

Poly(ethylene glycol)-diacrylate (PEGDA) hydrogels are widely used to mimic the microenvironment of human organ cells due to their tunable mechanical properties, ease of fabrication by radical polymerization, and low cytotoxicity. Developing PEGDA hydrogels in different sizes and shapes can eventually be used as a construct substrate for culturing of human stem cells by controlling the mechanical properties of the printed constructs and incorporating microstructures to facilitate cell growth. Previously fabrication of PEGDA hydrogels has been done with photolithography by using scaffold masks to control the crosslinking pattern in multiple layers. However, this method is labor-intensive and not scalable to production scale. 3D printing by micro-stereolithography enables faster and reproducible manufacture.

MANUFACTURING

Shaping the PEGDA constructs using 3D stereolithography printing makes it possible to produce them in a fast and efficient manner and gives the opportunity to produce multiple constructs at a time, thus making it industrially useful.

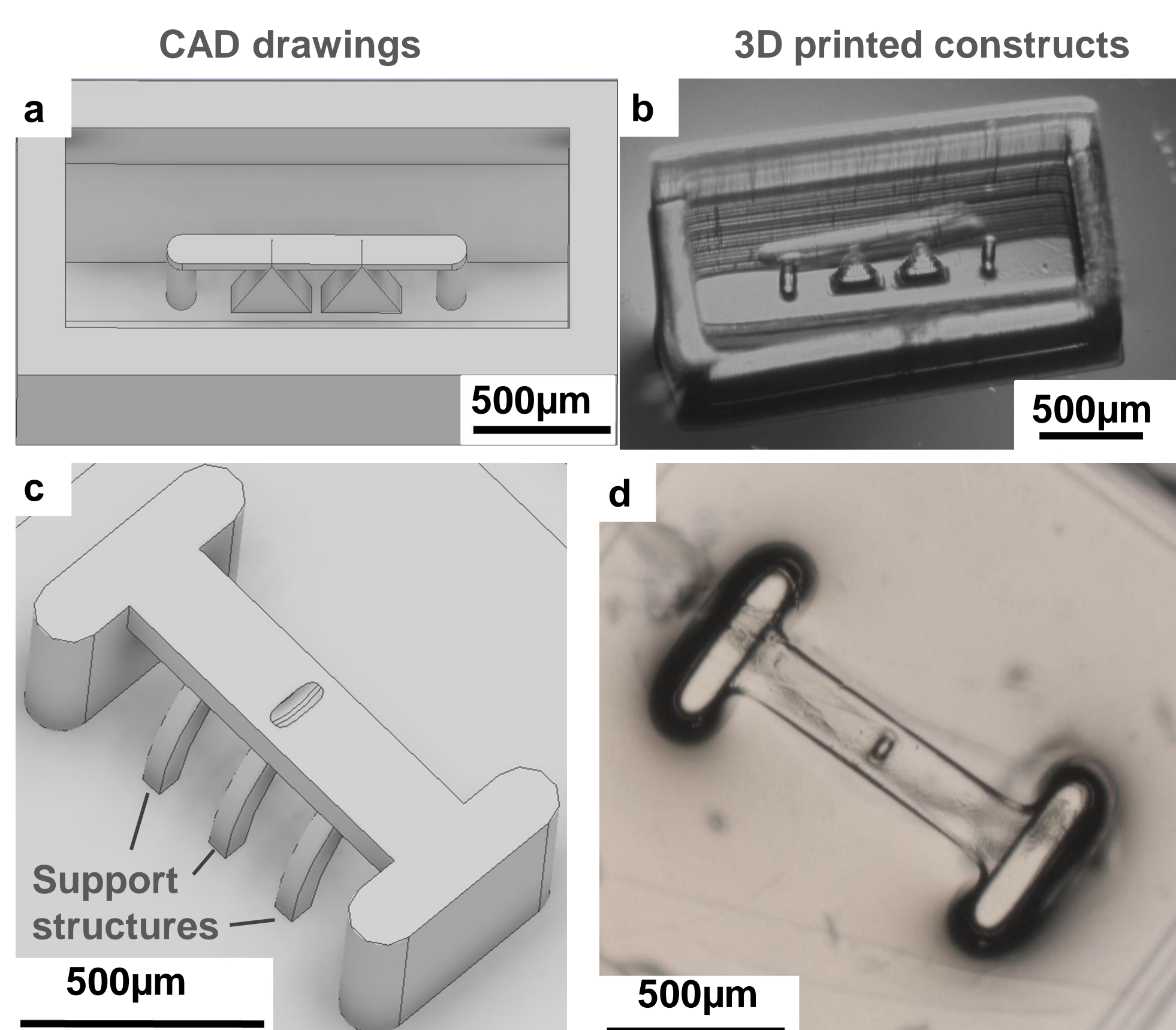


Figure 1. Manufacturing of 3D PEGDA constructs. (a,b) CAD drawing of targeted design showing triangular (a) and arched (b) support structures. (c,d) Resulting 3D printed PEGDA constructs.

Support structures can be printed in different shapes and dimensions based on their purpose (Fig. 1a,b).

It is possible to print support structures down to 40 µm in thickness allowing the main structure to be printed but without the support structures remaining in the final construct (Fig. 1c,d). This ability enables printing of larger free-hanging structures.

CELL CULTURING

The ability to incorporate more complex microstructures with feature sizes down to 40 µm enhances the possibilities to direct cell growth (Fig. 2a,b) and tissue formation by implementing mechanical cues (Fig. 2c).

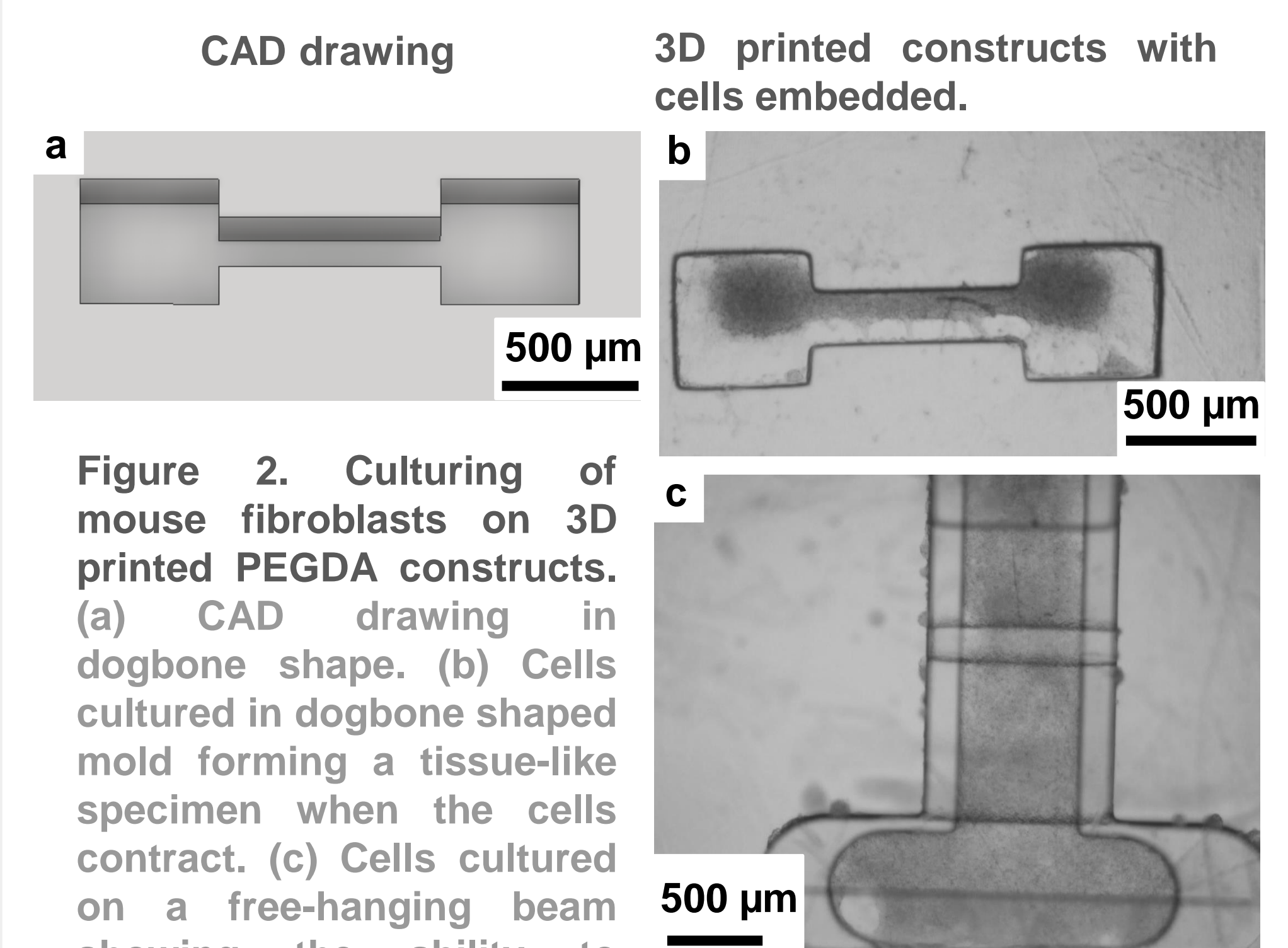


Figure 2. Culturing of mouse fibroblasts on 3D printed PEGDA constructs. (a) CAD drawing in dogbone shape. (b) Cells cultured in dogbone shaped mold forming a tissue-like specimen when the cells contract. (c) Cells cultured on a free-hanging beam showing the ability to position a cell-solution on the top of a 3D printed structure.

TESTING OF MECHANICAL PROPERTIES

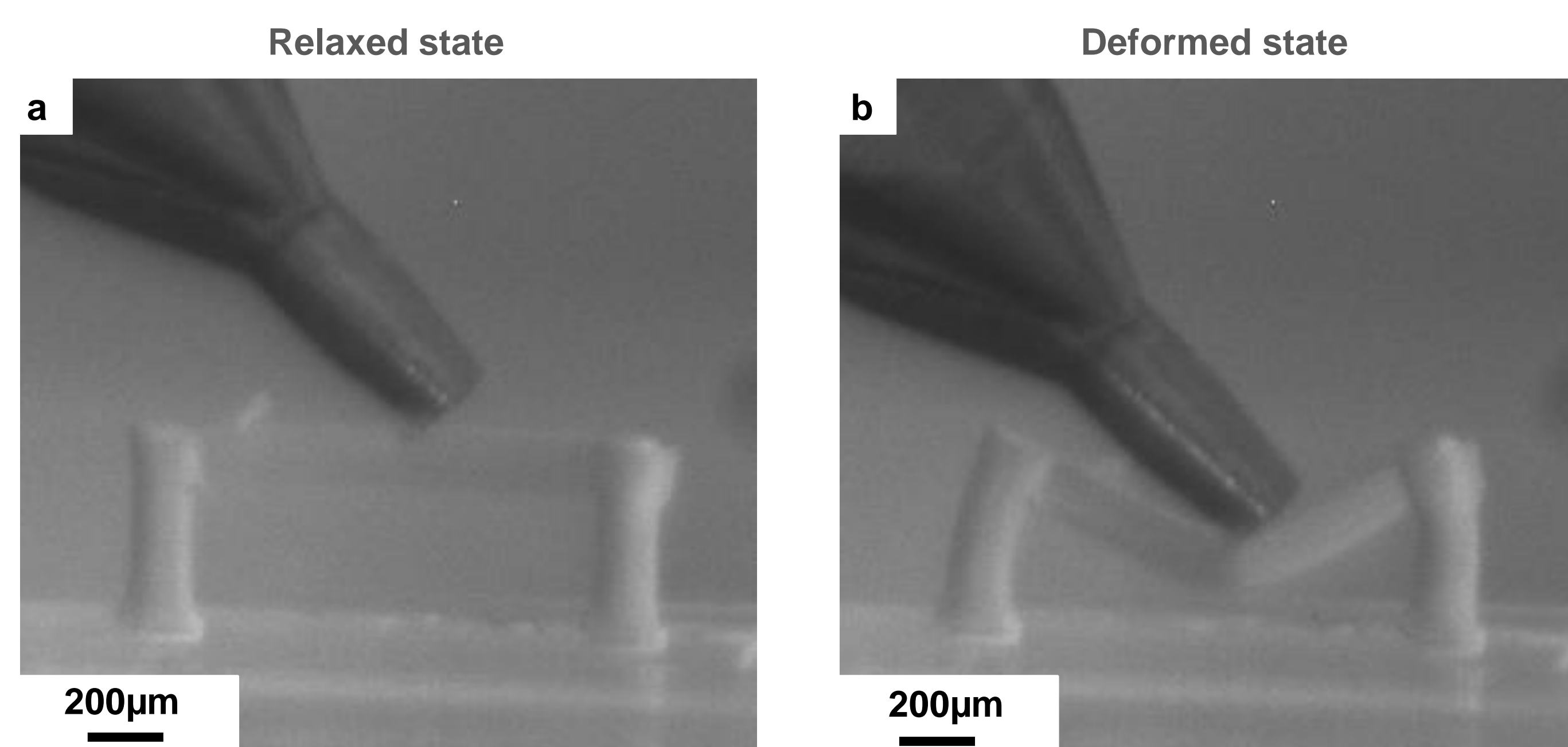


Figure 3. Mechanical testing of 3D printed construct. (a) Relaxed state of free-hanging beam with piezo controlled metal rod positioned at the surface. (b) 200 µm vertical displacement of free-hanging beam in the 3D printed construct by mechanical actuation executed by a piezo actuator.

Mechanically compliant constructs should be able to sustain repeated deformation as experienced in the body. Cyclic actuation of the PEGDA construct is done by using a piezo actuator that has been adapted to work in an aqueous environment and is coupled to an optical readout system with the possibility to connect to a force read-out system as well (Fig. 3). We have shown that the construct is able to withstand at least 1 million cyclic actuations without visual damages in the PEGDA hydrogel.